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UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/635,241	08/05/2003	Zhen Zhang	58369 (71699)	6657

21874 7590 09/11/2007 EDWARDS ANGELL PALMER & DODGE LLP P.O. BOX 55874 BOSTON, MA 02205	**EXAMINER**	
	DEJONG, ERIC S	

ART UNIT	PAPER NUMBER
1631	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

	Application No.	Applicant(s)
Office Action Summary	10/635,241	ZHANG ET AL.
	Examiner	Art Unit
	Eric S. DeJong	1631

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.
- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 May 2007*.

2a)☐ This action is **FINAL**.   2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

    4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *See Continuation Sheet* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

    Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

    Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

    a)☐ All   b)☐ Some *   c)☐ None of:

      1.☐ Certified copies of the priority documents have been received.

      2.☐ Certified copies of the priority documents have been received in Application No. _____.

      3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

    * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)

2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3)☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.

4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date _____.

5)☐ Notice of Informal Patent Application

6)☐ Other: _____.

DETAILED OFFICE ACTION

This application has been transferred to a new examiner.

Applicants response filed 05/02/7002 is acknowledged. Claims 1-111, 119, 121, 122, 125, 126, 128-130, 135, 136, 140, 146, 154-160, 162-164, 169, 170, 174, 179, 191, 193-195, 198, 199, 201-203, 206-209, 213, and 218 are canceled. Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157, 158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212, 214-217, and 219-224 are pending and currently under examination.

Claim Objections

The objection to claim 112 for minor informalities is withdrawn in view of amendments made to the instant claims.

Claim Rejections - 35 USC § 112

The rejection of claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145, 147-148, 182-190, 192, 196-197, 200, 204-207, 210-212, 214-217, and 219-224, under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in view of amendments made to the instant claims.

The rejection of claims 112-118, 120, 123-124, 127, 131-134, 137-139, 141-145,

147-153, 157-158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204,

205, 210-212, 214-217, and 219-224 under 35 U.S.C. 112, second paragraph, as being

indefinite is withdrawn in view of amendments made to the instant claims.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 149-153, 157, 158, 161, 165-168, 171-173, 176-178, 180-190, 192, 196,

197, 200, 204-207, 210-212, 214-217, 219, and 220 are rejected under 35 U.S.C. 101

because the claimed invention is directed to non-statutory subject matter. This rejection

is newly applied.

Regarding data structures representing descriptive material and computer

programs, MPEP § 2106.01(I) states:

"Data structures not claimed as embodied in computer-readable media are descriptive material per se and are not statutory because they are not capable of causing functional change in the computer. See, e.g., Warmerdam, 33 F.3d at 1361, 31 USPQ2d at 1760 (claim to a data structure per se held nonstatutory). Such claimed data structures do not define any structural and functional interrelationships between the data structure and other claimed aspects of the invention which permit the data structure's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a data structure defines structural and functional interrelationships between the data structure and the computer software and hardware components which permit the data structure's functionality to be realized, and is thus statutory.
    Similarly, computer programs claimed as computer listings per se, i.e., the descriptions or expressions of the programs, are not physical "things." They are neither computer components nor statutory processes, as they are not "acts" being performed. Such claimed computer programs do not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized. In contrast, a claimed computer-readable medium encoded with a computer program is a computer element which defines structural and functional interrelationships between the computer program and the rest of the computer which permit the computer program's functionality to be realized, and is thus statutory. See

Lowry, 32 F.3d at 1583-84, 32 USPQ2d at 1035. Accordingly, it is important to distinguish claims that define descriptive material per se from claims that define statutory inventions."

Claim 149 recites the limitation "A computer readable program product comprising a written... physical media" in lines 1 and 2 of said claim, which reads on a written computer listing that does not define any structural and functional interrelationships between the computer program and other claimed elements of a computer which permit the computer program's functionality to be realized. Rather, the written computer listing as instantly claimed encompasses nonfunctional descriptive material, *per se*, and is therefore not statutory subject matter. Claims 150-153, 157, 158, 161, 165-168, 171-173, 176-178, 180, and 181, which depend from claim 149, are also included under this rejection.

Claims 149-153, 157, 158, 161, 165-168, 171-173, 176-178, 180-190, 192, 196, 197, 200, 204-207, 210-212, 214-217, 219, and 220

Claims 149-153, 157, 158, 161, 165-168, 171-173, 176-178, 180-190, 192, 196, 197, 200, 204-207, 210-212, 214-217, 219, and 220 are drawn to a computer program product and related system comprising input data and computer instructions for performing the abstract and computation process steps of qualifying common data elements and selecting an intersection subset of data elements and, therefore, involves the application of a judicial exception. Regarding inventions involving the application of a judicial exception, said application must be a practical application of the judicial exception that includes either a step of a physical transformation, or produces a useful, concrete, and tangible result (State Street Bank & Trust Co. v. Signature Financial

Group Inc. CAFC 47 USPQ2d 1596 (1998), AT&T Corp. v. Excel Communications Inc. (CAFC 50 USPQ2d 1447 (1999)). In the instant claims, there is no step of physical transformation that results from said application of judicial exception, thus the Examiner must determine if said application of a judicial exception produces a useful, concrete, and tangible result.

In determining if the application of a judicial exception produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a result to be "useful," the application of a judicial exception must produce a result that is specific, and substantial. For a result to be "concrete," the application of a judicial exception must have a result that is reproducible. For a result to be "tangible," the application of a judicial exception must produce a real world result . Furthermore, the claim must be limited only to statutory embodiments.

Claims 149-153, 157, 158, 161, 165-168, 171-173, 176-178, 180-190, 192, 196, 197, 200, 204-207, 210-212, 214-217, 219, and 220 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application of a judicial exception to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the application of a judicial exception is outputted to a display, a user, a readily accessible memory or other computer on a network, or by including a physical transformation that results from the recited application of a judicial exception.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all

obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of

the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g)

prior art under 35 U.S.C. 103(a).

Claims 112-117, 123, 124, 127, 131-134, 137-139, 141, 143-145, 147, 148, and

221-224 is rejected under 35 U.S.C. 103(a) as being unpatentable over Petricoin (*The*

Lancet, 359:572-577 (February 16, 2002)) in view of Golub (*Science*, 286:531-537 (Oct.

15, 1999)).

Petricoin discloses analyzing two biological state classes – "unaffected" and

"affected" wherein the affected group is known to have cancer. Petricoin discloses

analyzing two independent sets of samples. Specifically, one "sample" is composed of

50 control samples for preliminary analysis, other 17 control samples, and samples from

cancer patients for preliminary analysis (*see* p. 572-573, Methods and *Study Population*; table 1; fig. 1, p. 575, and p. 576). Thus, the analysis of the original test data is analysis of "the first set" of samples. A second "sample set" is composed of 50 control samples for the masked analysis, other unaffected samples, and benign disease control samples (p. 573-573; fig. 1, p. 575, and p. 576). Petricoin teaches that results from the test (masked data) may be added to the model/dataset to improve prediction (p. 576, right col., third full paragraph). Therefore, Petricoin discloses that both "samples" were collected and separately statistically analyzed to classify samples into different biological states (*e.g.*, cancer and unaffected states) (fig. 1, p. 575, table 2, p. 576, left col.) AND also discloses an "intersection" subset (the totality of the data used for classification after "improvement"). Also, the results obtained from two independent samples (preliminary and masked) were "intersected" wherein data elements (key values for classifying samples, *e.g.*, M/Z) in the intersection subset is a member of both subsets (preliminary and masked samples) (p. 576). Petricoin teaches selecting a first subset of data elements from the first data (key M/Z values) (fig. 1 and p. 575 and 576). Petricoin further discloses a preanalytical variable, *e.g.*, medical status, a clinical characteristic, medical condition (*e.g.*, premenopausal, menopause, age, benign diseases, *etc.*) and age distribution (*see* table 1, p. 573, p. 576). Petricoin discloses samples collected at different locations (*e.g.*, 100 control samples were provided from NOCHDP clinic in Chicago, IL, and 17 other control samples were provided by the Simone Protective Cancer Institute in Lawrenceville, NJ, p. 572-573). Petricoin teaches using different assays for training and validation (masked) data wherein "masking" adds

an additional step to the method (p. 575, left col.). Petricoin discloses reshuffling

(resampling) of the two highest rated sets to form new subset candidates (p. 575).

Petricoin discloses selecting candidate biomarker (CA125) and testing it on a validation

data set (masked serum samples, p. 575 and p. 577). Petricoin discloses a biological

state is a characteristic of presence of a disease (cancer) and a biomarker is a

diagnostic of a disease (CA125). Petricoin teaches that values of data elements

represent level of components (proteins, p. 572, right col.) in a data point sample (M/Z

values determined by MS, p. 573; see also peaks on fig. 2). Expression of a law-

molecular-weight protein (a cancer antigen CA125) is measured by coupling serum

samples with a C16 hydrophobic interaction protein chip array (an immobilized capture

affinity array) and the amount of the protein is measured by SELDI-TOF mass

spectrometry (p. 573, right col.). The sample of Petricoin is serum and data collected

from serum relate to the cellular localization of components in a sample (*e.g.*,

components located in a soluble cell fraction or "attached" to suspended cell

membranes) (p. 573, left col.). Petricoin teaches using different assays for training and

validation (masked) data wherein "masking" adds an additional step to the method (p.

575, left col.). Petricoin also discloses "pattern-recognition" (p. 576, right col., third full

paragraph, line 10). Petricoin discloses a "classification" as a pattern recognition

process (fig. 1; p. 575, left col.).

Petricoin does not specifically teach selecting a second subset and displaying the

intersection subset.

Golub discloses a method for classifying cancer by using gene expression
monitoring (p. 531). Golub discloses using two classes (ALL and AML acute leukemia)
and two samples comprising both classes (38 initial leukemia samples and
independently collected 34 leukemia samples) (p. 532, 534). Golub discloses selecting
"predictors" from the first sample (38 samples) and testing the predictors on an
independent 34 leukemia samples (p. 532). Golub further discloses prediction strengths
for both the initial (cross-validation) sample and an independent sample and selection of
data elements with high prediction strength for both samples (selecting a first and a
second subset) (p. 543 and fig. 3). Golub also discloses comparing two samples
wherein the structure (data elements – gene predictors) in the initial sample is also seen
in the independent sample (i.e., samples are intersected) (p. 534, middle col. and fig.
4). Golub discloses displaying the intersection (fig. 3). Golub discloses that different
types of samples, bone marrow and blood, were collected by different protocols (e.g.,
samples from SJCRH were processed with a very different protocol) (p. 536-537,
paragraph 23). Also, collection of bone marrow and blood requires different protocols.
Golub discloses collecting samples at different collecting sites and from different
populations (p. 536-537, paragraph 23).

It would have been obvious to one skilled in the art at the time of the invention to
modify the method of Petricoin to select both a first and a second subset of data
elements and display the intersection, as taught by Golub, where the motivation would
have been to test a model/hypothesis and to compare results from a model and a test,
as taught by Golub, p. 534.

Claims 112-118, 120, 123, 124, 127, 131-134, 137-139, 141-145, 147-153, 157,

158, 161, 165-168, 171-173, 175-178, 180-190, 192, 196, 197, 200, 204, 205, 210-212,

214-217, and 219-224 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Petricoin (*The Lancet*, 359:572-577 (February 16, 2002)) in view of Golub (*Science*,

286:531-537 (Oct. 15, 1999)), as applied to claims 112-117, 123, 124, 127, 131-134,

137-139, 141, 143-145, 147, 148, and 221-224 above, and in further view of Barnhill

(U.S. Patent 6,789,069).

Petricoin and Golub make obvious claims 112-117, 123, 124, 127, 131-134, 137-

139, 141, 143-145, 148, and 221-224, as set forth above.

Petricoin also discloses using mass spectrometry (*i.e.*, SELDI) for acquiring and

processing experimental data and bioinformatics software for processing data (p. 573

and 575). Petricoin discloses a computer based chip system (the Protein Biology

System 2 SELDI-TOF mass spectrometer such as Ciphergen Biosystems with a

detector and a chip reader, p. 573). Petricoin also discloses that data were collected

and were used later for analysis (*i.e.*, data are stored).

Petricoin and Golub do not disclose a supervised learning algorithm and

specifically, a support vector machine analysis; protein binding partners in an

expression profiling assay; and a computer system and a computer readable medium

for performing the method.

Barnhill discloses a method for classifying unknown samples using a learning

machine, similar to that of Petricoin. Barnhill discloses different methods for data

acquisition such as nucleic acid arrays and protein expression assays (*e.g.*, antibody

chips to identify specific proteins, col. 13, line 5-15). Barnhill method comprises acquiring expression data and processing data via creating training set by using a support vector machine and using the set to classify unknown data (col. 5, line 1-54). Barnhill discloses a gene chip, a mass spectrometer, and a protein binding assay comprising a protein binding partner (col, 1-2 and col. 13, line 5-15).

Barnhill discloses a computer system and a program for executing his method wherein data are entered into a computer system via a user interface (col. 22, line 27-67 and fig. 10-12), qualified, and selected (see for a general description of a computer system and programs col. 21, line 27 – col. 26, line 38 and fig. 10-12). The system comprises a processor, an input device, a memory, programs, and a network connector (fig. 10). Example 1 illustrates the method and the system for executing the method of Barnhill wherein tables 2-4 represent a database of ranked data obtained during the execution of the method (col. 38-42).

It would have been obvious to one skilled.in the art at the time of the invention to modify the method of Petricoin and Golub to use a supervised learning algorithm and specifically, a support vector machine analysis, as taught by Barnhill, where the motivation would have been to improve pre-and post-processing data and maximize the value of genomic and proteomic information, as taught by Barnhill, col. 4, line 29-33. It would further have been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a protein expression assay, as taught by Barnhill, where the motivation would have been to determine efficiently specific proteins from a large protein expression pool, as taught by Barnhill (col. 12, line 10 –

col. 13, line 15). It would have also been obvious to one skilled in the art at the time of the invention to modify the method of Petricoin and Golub to use a computer and a computer readable medium for executing Petricoin's method, as taught by Barnhill, where the motivation would have been to manage large amount of complicated data in genomic and proteomic investigations, as taught by Barnhill, col. 1-2.

Response to Arguments

Applicant's arguments filed 05/02/2007 have been fully considered but they are not persuasive.

In regards to the rejection of claims under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and under 35 USC 103(a) as being unpatentable over Petricoin in view of Golub and in further view of Barnhill, applicants argue that Petricon does not suggest including the selection of an intersection subset. Applicants further argue that neither Golub nor Barnhill disclose or suggest "selecting an intersection subset of data elements from the first and second subsets" as applicants claim.

Applicants argument is not persuasive. It is reiterated from the above rejection that Petricoin teaches discloses analyzing two independent sets of samples and that the results from tests (masked data) may be added to the model/dataset to improve prediction (p. 576, right col., third full paragraph), which reads on selecting an intersection subset of data elements from the first and second subsets as instantly claimed.

Applicants further that Galub reports that sample preparations should be standardized, thereby teaching away from applicants method whereby independent discovery data sets may be collected from different locations or from using different collection protocols.

Applicants argument is not persuasive. It is reiterated from the previous Office action, mailed 11/02/2006, that Golub discloses a range of samples, *e.g.*, bone marrow and peripheral blood samples, samples collected from children and adults, samples collected from different labs, and samples collected by different protocols (p. 532, right col., last paragraph). Contrary to applicants argument, the explicit teaching from Golub of using different sample preparation protocols (p. 532, right col., last paragraph), encompasses independent discovery data sets that may be collected from different locations or from using different collection protocols.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. DeJong whose telephone number is (571) 272-6099. The examiner can normally be reached on 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Moran Marjorie can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

applications may be obtained from either Private PAIR or Public PAIR. Status

information for unpublished applications is available through Private PAIR only. For

more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business

Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO

Customer Service Representative or access to the automated information system, call

800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Eric S DeJong
Examiner
Art Unit 1631

08/24/2007

Continuation of Disposition of Claims: Claims pending in the application are 112-118,120,123,124,127,131-134,137-139,141-145,147-153,157,158,161,165-168,171-173,175-178,180-190,192,196,197,200,204,205,210-212,214-217 and 219-224.

Continuation of Disposition of Claims: Claims rejected are 112-118,120,123,124,127,131-134,137-139,141-145,147-153,157,158,161,165-168,171-173,175-178,180-190,192,196,197,200,204,205,210-212,214-217 and 219-224.